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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/527,440	03/17/00	NAKAE H	HIRA.0003

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1631	4

DATE MAILED: 06/21/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/527,440	NAKAE ET AL.	
	Examiner	Art Unit	
	Nancy Ogihara	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☒ Claim(s) *1 and 10* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be direction to Group Art Unit **1631**.

Preliminary amendment

Claims 1-12 are pending in the instant application. Applicant's preliminary amendment canceling claims 13-18 is acknowledged.

Claim Objections

Claims 1 and 10 are objected to because of the following informalities: In claim 1, the term "controling" is misspelled. The correct spelling should be "controlling." In claim 10, the term "collelated" is misspelled. The correct spelling appears to be "correlated." Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 9-10 are rejected under 35 U.S.C. §101 because the claimed invention is directed to non-statutory subject matter and is therefore not patentable. See MPEP §2106 which states "When nonfunctional descriptive material is recorded on some computer-readable medium, it is not structurally and functionally interrelated to the medium but is merely carried by the medium. Merely claiming nonfunctional descriptive material stored in a computer-readable medium does not make it statutory. Such a result would exalt form over substance." In the claims, the computer-readable medium is merely storing recorded data on polynucleotides used as primers and is therefore not statutory subject matter.

Claim Rejections - 35 USC § 112

Claims 3-5 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 3, applicant claims selection conditions "related to GC content and/or Tm." The term is vague and indefinite since the metes and bounds of the term "related" are unclear. The range of related nucleic acid sequences encompassed by the claim is not clear, since nucleic acids related to GC content can have any amount of GC content, including none at all, and still be considered as "related to GC content." Therefore, virtually any selection condition can be related to GC content, and therefore, says nothing about the selection method.

Claim 4 recites the limitation "said prescribed base length." There is insufficient antecedent basis for this limitation in the claim because no where in base claim 1 is there recited a base length.

In claim 5, the phrase "further controls of third selecting means" is confusing, and it is unclear what applicant intends. Furthermore, there is insufficient antecedent basis for the limitation of "third selecting mean" because base claim 1 recites only a first selecting means. There is a resulting gap in the sequential use of selecting means.

In claim 10, the phrase "which are collelated each other" is confusing. Does applicant intend to recite "correlated with each other"?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Sninski et al (U.S. Patent No. 5,176,995).

The claims are directed towards a primer design system comprising a receiver for obtaining data on DNA sequences and a control unit for extracting partial sequences of certain lengths, detecting certain conditions related to positions of the sequences, selecting partial sequences, and determining the sequence of primers capable of hybridizing.

Sninsky et al disclose a primer design system for PCR amplification comprised of using a commercially available computer program (i.e. a "receiver" or a computer-readable storage medium) from the National Biomedical Research Foundation (NBRF) in which a plurality of nucleic acids sequences from various related viruses is input by a user for sequence alignment and comparison (see

column 6, lines 4-12). Sninsky et al disclose SUNY Regional Oncology Center (Example 1) and Albert Einstein College of Medicine (Example 6) as databases from which viral sequences were obtained and input to the primer design system. A user-defined window size of greater than 6 base pairs was used for examining base pair homology, wherein the program employed a graphical interface to display a dot-plot representing regions of substantial homology (column 6, lines 11-14). Sninsky et al disclose that highly conserved regions within the aligned sequences are the preferred regions from which to select primers that specifically hybridize to a given sequence (see column 6, lines 21-24). This is illustrated in Figure 1 where several primers (i.e. a plurality) were designed that correspond to conserved sequences within the coding region (i.e. exon) of the gag protein of the AIDS virus. Sninsky et al further disclose that additional criteria for selecting nucleotide sequences (i.e. 2nd, 3rd, 4th, etc… selecting means) of primers include low homology to potential contaminating sequences, lack of secondary structure, and a preferable GC content of approximately 50% (see column 10, lines 35-65). In addition, further selection means can comprise using different combinations of the designed primers, as shown in Figure 1, to select and extract partial nucleotide sequences from the gag gene of various AIDS viruses. As disclosed in Examples 1 and 6, the designed primers were synthesized and subsequently used in a PCR amplification reaction (column 18, lines 31-49) for analysis of the different strains of AIDS virus. The computer program and method steps of Sninsky et al thus read on a system and method comprising detection of conditions, (eg. high sequence homology) related to the positions of partial sequences, selection of partial sequences meeting said detecting conditions (eg. high sequence homology), extraction of partial sequences meeting certain base length conditions (eg. window size), and determination of a primer sequence capable of specifically hybridizing to a plurality of DNA sequences. Furthermore, it is noted that the recitation of the term "kit" in the preamble of claims 11-12 is considered to be a statement of intended use and is accorded patentable weight only to the extent that it imposes limitations on the actual components of the kit. Given the above, the methods and system of Sninsky et al meet the limitations of the claims.

Claims 1, 4, 7-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Kariko (BioTechniques, vol 18(6), pp. 1048-1049, 1995).

Kariko disclose a primer design system for PCR amplification comprised of using the commercially available computer program MacDNASIS (i.e. a "receiver" or a computer-readable

storage medium) in which six different platelet-derived growth factor-A (PDGF-A) cDNA sequences were input by a user for sequence alignment and comparison (see page 1048, right column to 1049 left column). Kariko disclose that the cDNA sequences were obtained from the GenBank sequence database (see Figure 1). A user-defined window size of 14 nucleotides was used for examining base pair homology, wherein the program employed a graphical interface to display dot matrices representing regions of perfect homology (page 1049, lines 7-25). Kariko used these consensus sequences to select two primers (i.e. a plurality) that specifically hybridize to a given sequence (see underlined sequences in Figure 1) shared by the six PDGF-A DNA sequences. The computer programs and methods of Kariko thus read on method steps comprising detection of conditions, (eg. high sequence homology) related to sequence positions, selection of partial sequences meeting said detecting conditions (eg. high sequence homology), extraction of partial sequences meeting certain base length conditions (eg. window size), and determination of a primer sequence capable of specifically hybridizing to a plurality of DNA sequences. Furthermore, it is noted that the recitation of the term "kit" in the preamble of claims 11-12 is considered to be a statement of intended use and is accorded patentable weight only to the extent that it imposes limitations on the actual components of the kit. Given the above, the methods and system of Kariko meet the limitations of the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in

order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kariko (BioTechniques, vol 18(6), pp. 1048-1049, 1995), as applied to claims 1, 4, and 7-12, in view of Sninsky et al (U.S. Patent No. 5,176,995).

The teachings of Kariko are set forth above.

Kariko do not teach of a primer design system comprising a second means for selecting DNA nucleotides sequences under conditions related to GC content.

Sninsky et al teach of a primer design system in which the criteria for selecting primer nucleotide sequences (i.e. selecting means) comprises low homology to potential contaminating sequences, lack of secondary structure, and a preferable GC content of approximately 50% (see column 10, lines 35-65) as such considerations would insure maximum PCR amplification of the specific gene of interest, particularly if a sample comprises a mixed population of DNA.

Given that 1) Kariko have taught of a primer design system, for PCR amplification comprised of using a computer program (i.e. a "receiver" or a computer-readable storage medium) in which a plurality of cDNA sequences obtained from the GenBank database was input by a user for sequence alignment, wherein a user-defined window size of 14 nucleotides was used for examining base pair homology, and wherein the homologous sequences were used to select a plurality of primers that specifically hybridize to a given sequence, and 2) that Sninsky et al have taught of additional selection criteria for selecting primer nucleotide sequences which incorporate considerations of low sequence homology to contaminating sequences, lack of secondary structure, and a 50% GC content, it would have prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the selection criteria of Sninsky et al with the primer design system of Kariko as such design considerations would insure optimal PCR amplification with minimal contamination. One of ordinary skill in the art would have been motivated to combine the primer design system of Kariko with the additional primer selection criteria of Sninsky et al as one would want to avoid non-specific low yield PCR amplification of their gene of interest.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Ogihara whose telephone number is (703) 308-9363. The examiner can be reached Monday-Friday from 8:30-6:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Michael Woodward can be reached at (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1631 by facsimile transmission. Papers should be faxed to Group 1631 via the PTO Fax Center located in Crystal Park I. The faxing of such papers must conform with the notice published in the Official 1Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Nancy Ogihara
June 15, 2000

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